Each of the fragments was inserted into the cleaved pGCSF plasmids (Fig.16) to provide a plasmid pGCSF-ΔIN having the LTR-LTR fragment incorporated therein (Fig.17) and a plasmid pGCSF-IN having the LTR-LTR-integrase fragment incorporated therein (Fig.18). Also, as a positive control, a baculovirus vector was used into which a feline G-CSF gene had been inserted according to standard methods using a baculovirus transfer vector pBacPAK1 (Clontech).

IN THE DRAWINGS:

Please delete drawings labeled FIG.6, FIG 7, FIG 16, FIG 17, FIG 18, FIG 19, FIG 23, and FIG 24, each on one sheet, as originally filed with the application.

Please insert substitute drawings labeled labeled FIG.6, FIG 7, FIG 16, FIG 17, FIG 18, FIG 19, FIG 23, and FIG 24, each on one sheet, provided at Tab A.

REMARKS

Applicants respectfully request entry of the Preliminary Amendment provided herewith for the purpose of correcting typographical and clerical errors in the originally filed specification, including the drawings. None of the amendments constitute new matter. The justification for correction of the typographical errors is self-evident.

The amendment on page 68 is to provide the correct primer name used in the pLTR43 PCR amplification reaction. This change is supported on page 64, lines 10-12, page 65, lines 22-26, and in FIG.7, where the primer named "NLSPO35" is referred to correctly.

The present amendment includes a request for entry of substitute drawings labeled "FIG.6", "FIG.7", "FIG.16", "FIG.17", "FIG.18", "FIG.19", "FIG 23", and "FIG 24". This request is in accordance with 37 C.F.R. § 1.121(d). Clean versions of the corrected drawings are provided at Tab A. Marked-up copies of the originally filed drawings showing the changes that are requested in red are provided at Tab B.

FIG.6 and FIG.7 show the cloning strategies of plasmids pLTR43 and pLTR435, respectively. Both of these figures show two *SalI* restriction endonuclease sites (indicated as "S") in the respective constructs. The *SalI* site adjacent to the 3' terminus of the chloramphenicol resistance selectable marker is a clerical error. The corrections made to FIG.6 and FIG.7 are to delete this *SalI* site. Following deletion of this site, there remains a single *SalI* site adjacent to

the 5' end of the LacZ open reading frame. Additionally, the corrections made to FIGs 16-19, and 23-24 are to delete the erroneous *Sal*I site designated as "S".

This amendment is supported at page 59, lines 23-24, where it is said in reference to FIG.11, "pLTR435 was cleaved at two locations by *Eco*RI, at no location by *Nhe*I, and at one location by *Sal*I." Support for this amendment can also be seen in FIG.4 and FIG.5. These figures are restriction maps of the pLTR43 and pLTR435 plasmids. These maps correctly indicate that the two plasmids each have only a single *Sal*I restriction site, which is adjacent to the LacZ gene.

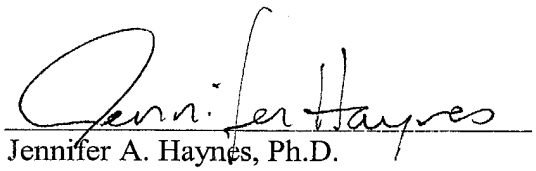
Attached hereto at the **APPENDIX** is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "**Version with markings to show changes made.**" Deleted text is shown with strike-through and new text is shown underlined.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: February 26, 2003

By: 

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APPENDIX

Version with markings to show changes made

IN THE SPECIFICATION:

The paragraph on page 53 spanning lines 1-17 has been amended as follows:

--(b) The methods for treating cancer using the vectors of the present invention also include treating cancer by introducing a drug metabolizing gene, also referred to as a suicide gene, into cancer cells. In this approach, a gene derived from microorganisms, which normally does not exist in the cells and encodes an enzyme involved in a certain metabolic pathway, is introduced by the vectors of the present invention into cancer cells. A prodrug (of an anti-microbial agent, in general) which is activated/exhibited cytotoxicity by the enzyme is then administered such that the cancer cells that have incorporated the gene are killed selectively. Examples of preferred combinations of a suicide gene and an associated prodrug include thymidine kinase (TK) gene of herpes simplex virus and gancyclovir ~~ganciclovir~~, TK gene of varicella-zoster virus and 6-methoxypurine arabinonucleoside ~~arabinoside~~, cytosine deaminase gene of *E. coli* and 5-fluorocytosine, and purinenucleoside phosphorylase ~~phospholyrase~~ of *E. coli* and 6-methylpurine-2'-deoxyriboside.--

The paragraph on page 68 spanning lines 5-8 has been amended as follows:

--The plasmid pLTR43 was cut by a restriction enzyme *Eco*RV, and a segment containing an integrase gene that had been amplified using IN53 and NLSPO35 ~~NLSPO~~ was ligated to the ends arising from the cutting by *Eco*RV to form a final plasmid pLTR435 (refer to Fig.5).--

The paragraph spanning page 71, line 17 through page 72, line 3 has been amended as follows:

--Fertilized eggs of white leghorn chicken of Line-M(C/O) described above, which were free from retroviruses, were incubated for 48 hours. On one side of each egg was formed a window having a diameter of about 1cm, through which a DNA-transferrin ~~tranferrin~~-poly L lysine complex prepared by the transferrinfection kit (*i.e.*, the same complex as that used in Example 2 for the purpose of the transfection ~~transferrinfection~~ into MEL cells) was injected into

the lower cavity of a blastoderm ~~blastderm~~ of embryos at a development stage in an amount of about 2ul/embryo using a glass capillary tube. The window was sealed with a strip of vinyl tape and incubation was continued until hatching. Blood samples were collected from the wing vein of the chicks two weeks after hatching.--

The paragraph spanning page 73, line 14 through page 74, line 3 has been amended as follows:

--A plasmid pGCSF was prepared b replacing the EGFP gene on the plasmid pEGFP-C1 (Clontech) with a feline G-CSF gene (Fig.15). The plasmid was cleaved with a restriction enzyme *Mlu*I. A fragment containing an LTR-LTR but not an integrase gene (which is referred to as an LTR-LTR fragment in Example 4) and a fragment containing an LTR-LTR-integrase gene region (which is referred to as an LTR-LTR-integrase fragment in Example 4) were cleaved out from the plasmid pLTR43 and pLTR435, respectively, with a restriction enzyme *Hinc*II. Each of the fragments was inserted into the cleaved pGCSF plasmids (Fig.16) to provide a plasmid pGCSF-ΔIN having the LTR-LTR fragment incorporated therein (Fig.17) and a plasmid pGCSF-IN having the LTR-LTR-integrase fragment incorporated therein (Fig.18). Also, as a positive control, a baculovirus vector was used into which a feline G-CSF gene had been inserted according to standard methods using a baculovirus transfer vector pBacPAK1 ~~pBac-PAK1~~ (Clontech).